REMARKS

Applicants request entry of the amendment and reconsideration of the rejection of the claims.

Applicants have cancelled claims 2-5, 7-13, and 23 without prejudice. Applicants reserve the right to pursue the subject matter of these claims in a continuation application. Applicants have amended claims 14, 30 and 38. Applicants submit the amendment is supported throughout the specification, including at page 3 lines 3 to page 4, line 14. Applicants submit that this amendment does not raise any issues of new matter.

35 U.S.C. § 112 rejection

In the Advisory Action, the Examiner rejected claims 23 and 38 under 35 U.S.C. § 112, first paragraph. The Examiner contends that while the specification is enabling for glycosylation site deletion variants it is not enabling for other glycosylation site variants. Claim 23 has been cancelled rendering the rejection moot. Claim 38 has been amended obviating the rejection.

Therefore, Applicants respectfully request withdrawal of the rejection.

35 U.S.C. §103

1) The Examiner rejected claims 2-4 and 10-13 under 35 U.S.C. § 103 as being unpatentable in view of Foster et al. in view of Ashkenazi et al. Applicants have cancelled those claims rendering this rejection moot.

2) The Examiner also rejected claims 2-5, 7-13, 15, 34-37 and 39-43 under 35 U.S.C. § 103(a) over Foster et al. in view of Ashkenazi et al. and Rickles et al. Applicants have cancelled claims 2-5, and 7-13 rendering the rejection of these claims moot. Applicants traverse the rejection with respect to the remainder of the currently pending claims.

Claim 34 is directed to a DNA construct comprising a nucleic acid sequence encoding a mammalian t-PA prosequence operatively linked to a nucleic acid sequence that encodes a presequence other than the mammalian t-PA presequence combined with a second nucleic acid sequence encoding a heterologous glycoprotein. As discussed in the specification at page 7, signal sequences include a presequence which directs the protein to the lumen of the ER and prosequence that directs protein to the Golgi apparatus.

Applicants submit that Foster in view of Ashkenazi and Rickles et al. do not make Applicants' claimed invention obvious, because with respect to claims 34-37 and 39-43, these references alone or together do not disclose all of the elements of the claimed invention.

As discussed previously, the Foster et al., Ashkenazi et al. and Rickles et al. do not teach or suggest the combination of a prosequence from a mammalian t-PA with a presequence other than the mammalian t-PA presequence. Foster et al. discloses the use of the entire signal sequence from t-PA. Foster does not disclose or suggest that the prosequence of a mammalian t-PA can be combined with a presequence other than the mammalian t-PA sequence.

The deficiencies of Foster et al. are not remedied by Ashkenazi et al. or Rickles et al. Ashkenazi et al. discusses TNFR-IgG, but does not teach or suggest any issues with secretion nor does it teach or suggest that any other signal sequence can or should be combined with TNFR-IgG.

Rickles et al. discloses isolation and purification of a cDNA encoding a murine tissue plasminogen activator as a probe to analyze t-PA expression. It does not disclose or suggest the combination of a t-PA prosequence with a heterologous presequence.

Thus, the combination of these references does not disclose all of the limitations of claims 34- 37, and 39-43. Thus, applicants respectfully request withdrawal of the rejection on this basis.

Claim 14 and 15 are directed to combining a DNA segment encoding a precursor polypeptide comprising a prosequence of a mammalian t-PA with a nucleic acid encoding a glycosylation deletion variant. These claims would not be obvious in view of the cited references because the references do not disclose all of the limitations of the claims.

None of the cited references teach or suggest glycosylation site variants. These references also do not indicate that glycosylation site variant glycoproteins have secretion problems or that using a prosequence from a mammalian t-PA would solve the problem. Secretion of glycosylation site variant glycoproteins represents different considerations than secretion of glycoproteins. Glycosylation is involved in signalling when a glycoportein is properly folded and ready for export to the Golgi apparatus. Deletion of glycosylation sites could affect processing and secretion of the protein. There is no teaching or suggestion in Foster et al. that the use of t-PA prosequence would work effectively to enhance secretion of glycosylation site variant glycoproteins.

Thus, Applicants respectfully request withdrawal of the rejection on this basis.

3) The Examiner rejected claims 2-4, 10-14, and 16-46 under 35 U.S.C. § 103(a) over Foster et al. in view of Ashkenazi et al. and Berman and Lasky. Claims 2-4, 10-13, 23 and 24 have been cancelled rendering the rejection moot with respect to these claims. Applicants traverse the rejection with respect to the remaining claims.

Applicants' arguments with respect to Foster et al. and Ashkenazi et al. cited above are incorporated in this rejection as well.

The Berman and Lasky reference do not remedy the deficiency of the references cited above. The Berman and Lasky reference is a general reference discussing expression of fully glycosylated proteins. The Berman and Lasky reference does not discuss or suggest any issues with secretion of glycoproteins and does not discuss glycosylation site deletion variants. This reference also not suggest combining a mammalian t-PA prosequence with a glycosylation site deletion variant or with a presequence other than a mammalian t-PA sequence to provide enhanced secretion.

Thus, Applicants respectfully request withdrawal of the rejection.

Applicants submit that the claims are in condition for allowance and notification to that effect is earnestly solicited.

Respectfully submitted,

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Date: November 21, 2001

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MARKED-UP VERSION SHOWING CHANGES

14. (Twice amended) A DNA construct comprising a first DNA segment encoding a precursor polypeptide comprising a prosequence of a mammalian t-PA and a second DNA segment operably linked to the first DNA segment, the second DNA segment, encoding a heterologous glycosylation site deletion variant glycoprotein.

30. (Twice amended) A cultured eukaryotic host cell comprising a DNA construct comprising: a first DNA segment encoding a precursor peptide [corresponding to a mammalian tissue plasminogen activator secretory peptide] comprising a prosequence of a mammalian t-PA; and a second DNA segment operably linked to the first DNA segment, the second DNA segment encoding a heterologous glycosylation site deletion variant.

38. The DNA construct of claim 34, wherein the heterologous glycoprotein is a glycosylation site deletion variant glycoprotein.